

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|                            |                             |
|----------------------------|-----------------------------|
| In re Application of:      | ) MONOHALOGENOVINYL VITAMIN |
|                            | ) D DERIVATIVE COMPOUNDS    |
| ANTONIO BUXADÉ VIÑAS et al | )                           |
|                            | ) Confirmation No. 3552     |
| Serial No. 10/579,594      | )                           |
|                            | ) Group Art Unit 1625       |
| Filed May 17, 2006         | ) Examiner Taylor V. Oh     |

DECLARATION OF ANGEL RAMON MESSEGUER PEYPOCH

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Angel Ramon Messeguer PeyPOCH, being duly sworn, hereby states and declares as follows:

1. I am an Organic Chemist. I obtained my PhD degree in 1974 at the University of Barcelona and I became staff member of the *Consejo Superior de Investigaciones Científicas* (Spanish Research Council-CSIC) in 1975. In 1991 I was promoted to Professor of Research of this public Institution. I am doing research in Bioorganic and Medicinal Chemistry at the Institute of Advanced Chemistry of Catalonia (IQAC-CSIC) and since 1995 I am director of this Institute. I have published over 170 papers in international journals and supervised over 20 Doctoral Theses; I am also coinventor of 18 patents. Several of these patents have been licensed to private companies of the pharma area. A compound discovered in our laboratory is currently in phase II clinical trials for anticancer treatment and it has been commercialised in the cosmetic field. I have been member of several national and international scientific and technologic panels devoted to evaluate R + D projects or patent disputes. In summary, I do have over 35 years of experience in the field related to bioactive organic compounds, their methods of preparation, characterization and activity.

2. I am fluent in both English and Spanish.

3. I have reviewed the above captioned Vinas *et al.* patent application.

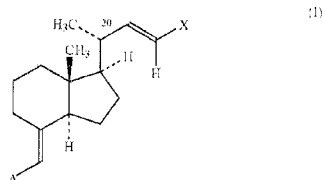
a. Specifically, I have reviewed:

i. the priority applications to the U.S. application: Spain Application No. 200302806 (filed November 28, 2003) and the PTC publication of the same application (WO 2005/051903) (both of which are in the Spanish language), and

ii. the corresponding U.S. Publication No. 2007-0129558 A1 (which is in the English language).

b. I have particularly reviewed the references in these documents to the 1999 TW Green book, namely paragraphs [0010] to [0013] of the U.S. publication as set forth below (as well as paragraphs [0019], [0020] and [0037]):

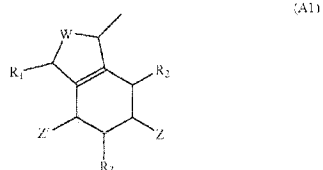
[0010] The new compounds correspond to general formula (I)



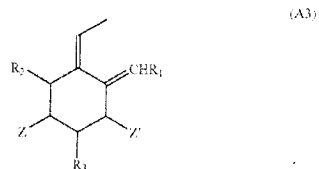
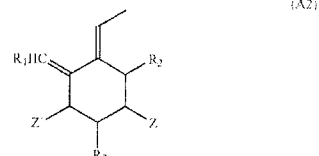
wherein:

[0011] X is an halogen atom selected from chlorine, bromine and iodine and

[0012] A is selected from any of the moieties corresponding to general formulas (A1), (A2) and (A3)



-continued



wherein:

[0013] Z and Z' are selected independently from hydrogen, a hydroxyl group and an —OR protected hydroxyl group, where R is a hydroxyl protective group; in a particular embodiment, R is any of the hydroxyl protective groups of those described in Green T W et al. "Protective groups in Organic Synthesis", Third Edition (1999), Ed. John Wiley & Sons (ISBN 0-471-16019-9);

This review has also included the references in the Spanish language priority applications, including the following paragraph which corresponds to paragraph [0013] of the U.S. application:

Z y Z' se seleccionan independientemente entre hidrógeno, un grupo hidroxilo y un grupo hidroxilo protegido-OR, en el que el R es un grupo protector de hidroxilo ; en una realización particular, R es cualquiera de los grupos protectores de hidroxilo descritos en Green TW et

al. "Protective groups in Organic Synthesis", Tercera Edición (1999), Ed. John Wiley & Sons (ISBN 0-471-16019-9);

4. The identification of the TW Green book is sufficiently specific for me to be able to identify and obtain the book. Further, it is my opinion that anyone of ordinary skill in the art of chemistry would be able to identify and obtain the book.

5. I have also reviewed the TW Green book.

a. Based on my review of the TW Green book as well as my skill in this art:

i. I readily understand that the reference to "any of the hydroxyl protective groups of those described in Green T W et al." specifically refers to the hydroxyl protective groups listed on pages 10-14 of the Green book.

ii. I understand the mention in the Vinas *et al.* patent applications of the hydroxyl protective groups described in to the TW Green book to clearly convey that those specific hydroxyl protective groups were intended to be incorporated as a part of the disclosure of the patent applications, and that the language was not intended to merely refer to the material. I particularly understood from the language of the Vinas *et al.* patent applications that the hydroxyl protective groups in TW Green were the full and complete list of such groups from which "R" in formulas (A1), (A2) and (A3) of the Vinas *et al.* patent applications could be selected, and that Vinas *et al.* intended for those groups to be a part of the disclosure of their invention.

iii. It is my opinion that the list of hydroxyl protective groups listed in pages 2-5 of Corrected Amendment "B" submitted during the prosecution of the Vinas *et al.* U.S. patent application is a complete and accurate identification of the hydroxyl protective groups found in the Green book referenced by the language in the above referenced Spain, PCT and U.S. patent applications.

b. It is my opinion that anyone of ordinary skill in the art of chemistry and the technology of the Vinas *et al.* patent application would also:

i. understand that the reference to "any of the hydroxyl protective groups of those described in Green T W et al." specifically refers to the hydroxyl protective groups listed on pages 10-14 of the Green book;

ii. understand the mention in the Vinas *et al.* patent applications of the hydroxyl protective groups described in to the TW Green book to clearly convey that:

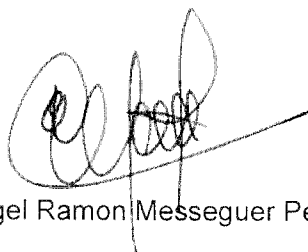
a) those specific hydroxyl protective groups were intended to be incorporated as a part of the disclosure of the patent applications, and that the language was not intended to simply generally refer to the material; and

b) the hydroxyl protective groups in TW Green were the full and complete list of such groups from which "R" in formulas (A1), (A2) and (A3) of the Vinas *et al.* patent applications could be selected, and that Vinas *et al.* intended for those groups to be a part of the disclosure of their invention; and

iii. recognize that the list of hydroxyl protective groups listed in pages 2-5 of Corrected Amendment "B" submitted in the prosecution of the Vinas *et al.* U.S. patent application is a complete and accurate identification of the hydroxyl protective groups found in the Green book referenced by the language in the above referenced Spain, PCT and U.S. patent applications.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

July 9, 2010



Angel Ramon Messeguer PeyPOCH